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# RAYLESS GOLDENROD (APLOPAPPUS HETEROPHYLLUS) AS A POISONOUS PLANT

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## HISTORICAL INTRODUCTION

The possible poisonous properties of rayless goldenrod *Aplopappus heterophyllus* (A. Gray) Blake,[1] were first brought to the attention of the Department of Agriculture in 1905, in a letter written by E. O. Wooton, then at Mesilla Park, N. Mex. He sent a specimen of the plant and stated that it was reported as a plant poisonous to cattle and horses if it had been frosted. One man was reported to have lost 22 horses in 10 days, just after the plant had been frosted. Other animals in the same pasture, however, were not affected. It was stated also that the horses did not eat it until after it had been frosted. Mr. Wooton wrote again to the department in 1907, referring to the belief among some of the stockmen that the plant made milk poisonous. It appears to have been thought by many at that time that the plant was the cause of the disease known throughout the Pecos Valley as alkali disease or milk sickness.

E. L. Moseley, (7)[2] in May, 1909, published in the Medical Record an article on the cause of "trembles" or "milk sickness," in which

[1] Formerly called *Isocoma wrightii*.
[2] Reference is made by number (italic) to "Literature Cited," page 24.

he upheld the theory that salts of aluminum caused the disease. He stated that he had isolated aluminum phosphate from some Aplopappus stems obtained from Wooton, and expressed his belief that the so-called alkali disease or milk sickness of the Pecos Valley was caused by aluminum phosphate in the plant.

In the Journal of Infectious Diseases, September, 1909, Jordan and Harris (*3*) published their article on milk sickness, which disease they thought was caused by a bacterium, called by them *Bacillus lactimorbi*. They mention the fact that the rayless goldenrod is believed by some to be the cause of the disease as it occurs in the Pecos Valley. In the same number of the publication mentioned, Luckhardt (*4*), in an article entitled "Additional Notes on the Bacteriology and Pathology of Milksickness," stated that he had found *B. lactimorbi* on the rayless goldenrod. Jordan and Harris and Luckhardt assumed that the plant was the carrier of the germ which produced the disease.

In 1914 L. M. Harrison, field agent of the Bureau of Statistics, United States Department of Agriculture, forwarded from Albuquerque, N. Mex., a letter from R. J. Freeland, of Logan, N. Mex., in which it was stated that cattle had been dying, and that some people thought it was from eating the plant, of which he sent a specimen, and which proved to be the rayless goldenrod.

In August, 1916, Dr. P. J. Smith, of Carlsbad, N. Mex., sent a sample of the weed to the department, stating that stock owners claimed that it produced symptoms similar to alkali poisoning, such as tremors, weakness, irritation of the intestines and kidneys, polyuria, and death if the animal is overheated by exercise.

In September, 1916, F. L. Schneider, of the Bureau of Animal Industry, inspector in charge at Albuquerque, N. Mex., sent a letter written by Doctor Kemper, of his force, and also a specimen of the rayless goldenrod. Kemper stated that the plant was called "rocea" by the Mexicans, that stock eat it mostly in winter and spring, and that the symptoms resemble those of turpentine poisoning, and appear, as a rule, only when the animals are worked or driven. The animals become fatigued rapidly, have an unsteady gait, drag their hind legs, have labored breathing, abdominal pains, great weakness, and if urged further, fall to the ground in convulsions, death following in from a few hours to two days.

In December, 1917, Clifton Carter, of the Bureau of Animal Industry, made an investigation of the matter at Grandfalls, Tex., and made the following report:

> I found, through conversation with a number of the cowmen and farmers at Grandfalls, that there had been a greater loss than usual among their livestock. A considerable number of work horses, stock horses, and cattle, both in the pasture and in the fields of the irrigated farms, had died. All agreed that there were no new symptoms, but that the loss is occasioned by the same cause which had killed stock in the Pecos Valley since its first settlement and had always been known as "alkali poisoning." The loss this year had been greater than usual. In this connection I feel that the fact that the drought had caused an extreme shortage of feed, and that the Pecos River is so low that the water is much more impregnated with salts than usual, should be taken into consideration.
>
> Owing to the fact that the loss in summer is not so great, very few of the residents consider the water the cause of the disease. Most of them with whom I talked think the rayless goldenrod, a sample of which I am forwarding

the department, is the cause. The loss is confined wholly to the valley, the stock drinking from the irrigating ditches or from wells nearly as strongly impregnated with salts. All the water for human consumption in this district is hauled from wells on the high land back from the river.

The symptoms of the disease, as described by the residents, are invariably the same. Usually the animals appear normal until they are exercised. When the horses are put in use or the cattle are moved from one point to another, an animal will suddenly become stiff, begin to tremble violently, and refuse to move. As reported, the temperature is subnormal, the pulse rapid. Horses sweat profusely in the early stages; sometimes the urine is streaked with blood. The animals often recover if permitted to rest; in other cases, after lingering for some days, they die. Some men stated that they would eat and drink until the last; others that they would take neither food nor drink.

The symptoms as described in the horse seemed to me strikingly similar to azoturia.

At the time of my arrival we could locate but one sick animal near Grandfalls. This was a yearling Durham steer, belonging to C. C. Dorr, about 4 miles south of Grandfalls. I visited Mr. Dorr's farm the afternoon of the 18th. He has a herd of 50 head or so of purebred Durham cattle, in good condition, running in the cotton stalks and alfalfa fields on his farm. The alfalfa is pastured to the ground, but the goldenrod, before mentioned, grows profusely on the banks of the canals and along the fence rows. The Mexican in charge of the herd stated that these cattle had been shut off from water for a day, went then into the canal and drank profusely. At the time I saw them, 5 p. m., there were no noticeable symptoms except in the case of the yearling mentioned. This animal was lying in the corral with its head to its side. Apparently it had not drunk for a day or two; temperature was 103, respiration 42, pulse 90. The animal was very weak, and upon being forced to its feet it trembled violently and staggered drunkenly about, lying down again at once. There was a thin, mucous discharge from the nostrils, the mucous membranes of which were inflamed, and the animal was apparently constipated, this latter seemingly being typical of the disease, especially in the latter stages.

I examined this animal the next day at 1 p. m. Respiration and pulse were practically the same, temperature 102.2. The animal appeared stronger, but had neither eaten nor drunk, nor were there visible signs of defecation.

The animal was still alive the morning of the 20th, apparently no worse, according to the owner, who did not wish him killed for post-mortem examination as long as there was a chance for recovery.

At the time of my last visit to this animal I obtained blood smears, which I am forwarding to the Pathological Division by mail, along with the so-called rayless goldenrod.[3]

Learning that W. G. Wynne, living some 5 miles north of Grandfalls, was losing some cattle, I visited his ranch the afternoon of the 19th. I found his cattle extremely emaciated and consequently not good subjects for post-mortem examination; however, I held a post-mortem on a 2-year-old heifer that had died that morning. The man in charge had driven her a mile or so the day before, when she exhibited symptoms of "alkali," as he expressed it. He had left her at an irrigating ditch, where she had drunk, lain down, and was dead next morning. Post-mortem examination revealed the most marked changes in the liver, which showed extreme icterus, the gall bladder being enormously enlarged. The bladder was distended with urine, which was of a citron-yellow color. I had noticed an excessive flow of urine from the Dorr calf.

In the Wynne heifer the kidneys showed degeneration, there were petechiæ in the lungs and heart muscle; the other tissues were not noticeably icteric; what fat remained had broken down into a gelatinous mass.

I would infer from the post-mortem examination that the animal had been subjected to a long-continued irritant poison, but whether of a vegetable or mineral nature I could not say.[4]

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[3] An examination of the blood slides by G. T. Creech, of the Pathological Division, Bureau of Animal Industry, showed no bacteria, and nothing abnormal except a slight distortion of the red corpuscles.

[4] Specimens of the liver were examined by G. T. Creech, of the Pathological Division, Bureau of Animal Industry. Cultures showed putrefactive organisms, but nothing resembling *Bacillus lactimorbi*. Sections were made, but decomposition had proceeded so far that no inferences could be drawn from their examination.

According to W. E. Baker, M. D., of Grandfalls, a person is taken violently ill with the disease, oftentimes when the cow which provided the milk does not show symptoms of alkali; again, a calf being fed the same milk will sicken at the same time. The symptoms, as Doctor Baker described them, are profound weakness, trembling, nausea and vomiting, extremely rapid heart action, subnormal temperature, and complete paralysis of the lower bowel. If the animal remains perfectly quiet, it usually recovers; if violently exercised, death usually results.

In 1920 Thornber and Brown (*8*, pp. 457–459) published a description of a loss of cattle in Arizona apparently from the rayless goldenrod, the plant being identified by them as *Bigelovia coronopifolia*, and reported a feeding experiment with a horse which produced no injurious effect.

Johnson and Archer (*2*, pp. 24–26) published a statement in 1922 giving the symptoms and pathological effects produced by the plant.

In the winter of 1922 and 1923, Dr. W. H. Enneis, health officer, Carlsbad, N. Mex., made a report to the department on some cases of human milk sickness and sent some tissues from a fatal case, which were examined in comparison with the animal tissues from the Aplopappus cases.

The foregoing comprises the information derived from literature and correspondence. Personal investigations by the writers have added somewhat to these statements and confirmed many of them.

The most serious complaints of the "alkali disease" or "milk sickness" are from the Pecos Valley, in the region from Roswell, N. Mex., to Fort Stockton, Tex. The trouble has been especially acute from Carlsbad, N. Mex., to Grandfalls, Tex. Popularly it is definitely connected with the "milk sickness" of human beings. There have been considerable losses of cattle and horses. It is generally believed that the disease is conveyed by milk and butter. So sure are the people of that fact that it is almost impossible to sell milk or butter from some Pecos Valley farms. The products are considered safe only when the cows are fed and are not allowed to run on pastures. To engage in the dairy industry is practically impossible in some localities.

Although the disease is especially prevalent in the Pecos Valley, it occurs in other localities in New Mexico and Arizona. The disease has had an especial interest, because by many it has been considered identical with the "milk sickness" or "trembles" known in the Central and Eastern States for more than a century, the cause of which has been definitely proved only within the last few years to be the plant *Eupatorium urticæfolium*, commonly known as white snakeroot. The symptoms produced in human patients by *Eupatorium urticæfolium* can not be distinguished from those produced by *Aplopappus heterophyllus*. Physicians from the milk-sick areas of the East have recognized the symptoms of western patients as identical with those that they have seen in their former homes. Doctor Doron, formerly of Patagonia, Ariz., made a diagnosis of cases occurring there from the description made in the diary of his grandfather, who had been a physician in Indiana.

The work of Jordan and Harris (*3*), already referred to, seemed to confirm this belief in the identity of the eastern and western diseases, and many have accepted the theory that plants have no connection with the disease except as mechanical carriers of the causal

bacterium. It has been shown, however, by Marsh and Clawson (*5*, *6*), Curtis and Wolf (*1*), and Wolf, Curtis, and Kaupp (*9*), that most cases of so-called milk sickness of domestic animals in the eastern United States are caused by *Eupatorium urticæfolium*. It may be interesting to note in this connection that the chemical study of these two plants by J. F. Couch, of the Bureau of Animal Industry, which is now in an advanced state, shows conclusively that the toxic substances in the two plants are not the same.

Inasmuch as the disease in the Pecos Valley has been generally considered as connected with the so-called rayless goldenrod (*Aplopappus heterophyllus*) and by many has been considered to be the result of intoxication by this plant, it was considered of great importance to determine conclusively whether the plant has toxic properties for livestock. It certainly is a very unusual state of things for two distinct plants, growing in widely separated parts of the country, to produce similar poisonous effects on domestic animals.

It was with the intention of proving definitely and finally whether *Aplopappus heterophyllus* was poisonous or not that the feeding experiments detailed in this bulletin were undertaken.

## DESCRIPTION OF THE PLANT[5]

*Aploppappus heterophyllus*, shown in Figure 1, belongs to the Composite family, in which the flowers are in compact heads, the heads being often mistaken for real flowers, as in the case of the sunflowers. It is commonly called rayless goldenrod, but in some localities the term "jimmy weed" is used.

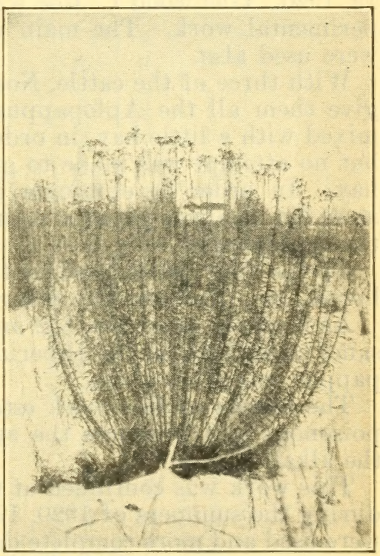

FIG. 1.—A single plant of *Aplopappus heterophyllus*

The plant is a stout, erect, tufted perennial herb with shrubby or near shrubby base, minutely hairy to nearly smooth, commonly from 1 to 2 feet in height, but sometimes under favorable circumstances of growth, as on the banks of irrigating ditches, it may reach a height of 4 feet or even more.

The leaves are alternate, linelike or broader, one-eighth to one-fourth inch wide, three-fourths to 2½ inches long, usually with stout, stiff hairs on the margin, occasionally with short, sharp, scattered teeth, and acute or obtuse at the apex.

The heads are numerous, with or without stems, in terminal flat-topped bunches; the bracts surrounding the flower heads are about one-eighth inch high, oblong, usually obtuse, with obscurely green tips. The heads have 7 to 15 tubular yellow flowers. The seeds are silky and small.

[5] The description of the plant was prepared by W. W. Eggleston, of the Bureau of Plant Industry.

The plant is found from southern Colorado to the Texas Panhandle and south to Arizona, Sonora, and Chihuahua. It grows in great abundance in the irrigated portions of the Pecos Valley in New Mexico and Texas.

## EXPERIMENTAL WORK

About the middle of October, 1919, the writers visited the Pecos Valley with the intention of making some detailed feeding experiments in order to determine definitely whether the plant was poisonous. After some preliminary investigations it was decided to carry on feeding work at Roswell, N. Mex., which seemed to be the most available place for the work. With the assistance and cordial cooperation of the county agricultural agent, J. R. Thomas, and of George A. Lipp, of the Bureau of Animal Industry, arrangements were made for the necessary experimental animals and accommodations for handling them, and the work was continued until January 19, 1920. Glenwood C. Roe was left in immediate charge of the experimental work. The main work was with cattle, but two horses were used also.

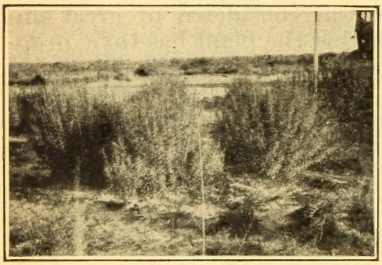

FIG. 2.—A group of plants of *Aplopappus heterophyllus*

With three of the cattle, Nos. 851, 853, and 854, it was planned to give them all the Aplopappus they would eat. The material was mixed with a little hay, in order to induce them to eat more readily, but no attempt was made to give them a maintenance ration of the hay. In order to eliminate definitely the question of starvation, steer No. 855 was given a maintenance ration of hay in addition to the Aplopappus.

Of the four cattle used in the experiment, all died. Of the two horses, one died and the other showed pronounced symptoms.

As controls, steer No. 852 and horse No. 134 were kept under the same conditions as the experimental animals, except that no Aplopappus was given them.

The results of this work established the fact that Aplopappus is poisonous and produces the symptoms considered characteristic of the alkali disease.

This work was continued at the Salina (Utah) experiment station during the summers of 1920, 1921, 1922, and 1923. Cattle and sheep were used and more complete data were obtained, especially in regard to symptoms, pathological effects, dosage, comparative toxicity of stems and leaves, possible remedies, and possibilities of transmission of the poison through milk.

A thorough chemical examination of the plant by J. F. Couch, chemist in the Pathological Division, cooperating in poisonous-plant investigations, is well advanced.

Table 1 gives a summarized statement of the results of the feeding experiments, 1919 to 1923, inclusive.

TABLE 1.—*Summary of feeding experiments with Aplopappus heterophyllus, 1919 to 1923, inclusive*

| Animal | | Date of feeding | Method of feeding | Part of plant used | Green plant given per 100 pounds of animal | | | Place and date of plant collection | Result | Remarks |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | Total | To produce sickness | | | | |
| Designation | Weight | | | | | Total | Daily dose | | | |
| Cattle Nos.: | *Pounds* | | | | *Per cent* | *Per cent* | *Per cent* | | | |
| 851 | 350 | Oct. 22-Nov. 4, 1919 | With hay | Stems, leaves, and flowers. | 9.428 | 9.428 | 1.35 | Roswell, N. Mex., fall of 1919. | Death | |
| 853 | 350 | Oct. 22-Nov. 3, 1919 | do | do | 13 | 8.85 | 1.47 | do | do | |
| 854 | 300 | do | do | do | 17 | 17 | 2.12 | do | do | |
| 855 | 410 | Nov. 20, 1919-Jan. 8, 1920. | do | do | 58.52 | 46.82 | 1.38 | do | do | |
| 856 | 370 | Oct. 22-Nov. 5, 1919 | do | do | 9.648 | 9.648 | 1.20 | do | do | |
| 892 | 739 | Aug. 5-24, 1920 | With hay and grass. | do | 32.82 | 9.742 | 1.95 | Roswell, N. Mex., Jan. 15, 1920. | Sick | |
| 893 | 156 | do | Milk from mother, No. 892. | | | | | | Symptoms | |
| 840 | 776 | Aug. 24-Sept. 12, 1920 | With hay | Stems, leaves, and flowers. | 30.34 | 15.46 | 1.82 | Roswell, N. Mex., Oct. 27, 1919, Jan. 6 and 15, 1920. | Sick | Remedy, pasture, bran, mash, and quiet. |
| 895 | 78 | do | Milk from mother, No. 840. | | | | | | Probable symptoms. | |
| 911 | 800 | June 19-July 21, 1921 | With hay | Stems, leaves, and flowers. | 33 | | | Roswell, N. Mex., December, 1920. | Not sick | Exercised twice. |
| 917 | 160 | do | Milk from mother, No. 911. | | | | | | Probable symptoms. | |
| 868 | 739 | Aug. 14-25, 1921 | With hay | Stems, leaves, and flowers. | 22.46 | 22.46 | 2.04 | Roswell, N. Mex., December, 1921. | Death | Remedy, green grass and strychnine. |
| 924 | 84 | Aug. 14-Sept. 1, 1921 | Milk from mother, No. 868. | | | | | | do | Given strychnine as remedy. |
| 877 | 520 | Aug. 29-Sept. 24, 1921 | With hay | Stems, leaves, and flowers. | 25 | | | Roswell, N. Mex., December, 1920. | Not sick | |
| 961 | 700 | Aug. 7-Aug. 21, 1922 | do | do | 16.06 | 16.06 | 1.46 | Roswell, N. Mex., October, 1921. | Death | Possible symptoms, Aug. 17. Trembling noted Aug. 24. Remedy, glucose, sodium bicarbonate. |
| 962 | 102 | Aug. 7-Aug. 26, 1922 | Milk from mother, No. 961. | | | | | | Not sick | Killed for autopsy. Normal as far as could be seen. |

TABLE 1.—*Summary of feeding experiments with Aplopappus heterophyllus, 1919 to 1923, inclusive*—Continued

| Animal | | Date of feeding | Method of feeding | Part of plant used | Green plant given per 100 pounds of animal | | | Place and date of plant collection | Result | Remarks |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | Total | To produce sickness | | | | |
| Designation | Weight | | | | | Total | Daily dose | | | |
| Horse Nos.: | *Pounds* | | | | *Per cent* | *Per cent* | *Per cent* | | | |
| 132 | 690 | Nov. 13–Dec. 3, 1919 | With hay | Stems, leaves, and flowers. | 16.37 | 15.21 | .84 | Roswell, N. Mex., fall, 1919. | Death | |
| 133 | 705 | Nov. 20, 1919–Jan. 19, 1920. | do | do | 50.62 | 17.852 | .99 | do | Sick | |
| Sheep Nos.: | | | | | | | | | | |
| 589 | 85 | June 25–July 22, 1920 | do | do | 31.294 | 12.048 | 1.50 | Roswell, N. Mex., Jan. 15, 1920. | Death | |
| 563 | 109 | July 31–Sept. 10, 1920 | do | Stems, leaves, and flowers, autoclaved. | 33.94 | 33.94 | .97 | do | Sick | Not fed Aug. 20, 21, and 22. |
| 566 | 89 | Aug. 8–Sept. 12, 1920 | Balling gun. | Stems, leaves, and flowers. | 19.76 | | | Roswell, N. Mex., Jan. 6 and 15, 1920. | Not sick | Kept in pasture. |
| 570 | 85 | Aug. 8–Sept. 22, 1920 | Balling gun and with hay. | do | 22.822 | | | do | Probable symptoms. | Not fed Aug. 20, 21, and 22. |
| 576 | 119.5 | Aug. 25–Sept. 26, 1920 | With hay | do | 36.82 | 36.82 | 1.27 | Roswell, N. Mex., Oct. 27, 1919. | Sick | |
| 373 | 119.25 | June 19–July 10, 1921 | With hay | do | 25.32 | 25.32 | 1.33 | Roswell, N. Mex., December, 1920. | Sick | |
| 655 | 17.5 to 23. | do | Milk from mother, No. 373. | | | | | | do | Drowned. |
| 495 | 128.25 | June 29–Aug. 18, 1921 | Balling gun. | Stems, leaves, and flowers. | 100 | | | Roswell, N. Mex., December, 1920. | Not sick | In pasture. |
| 656 | 18.25 to 45. | do | Milk from mother, No. 495. | | | | | | do | During latter part of experiment nibbled grass. |
| 701 | 96.5 | June 21–July 9, 1922 | Balling gun | Stems, leaves, and flowers. | 34 | 28 | 1.64 | Roswell, N. Mex., October, 1921. | Death | Kept in pasture. Symptoms July 7. Remedy, sodium bicarbonate, Glauber salt, whiskey. |
| 700 | 15 | do | Milk from mother, No. 701. | | | | | | do | Symptoms July 6. Remedy, sodium bicarbonate. |
| 641 | 107 | June 25–June 29, 1922 | With hay | Stems, leaves, and flowers. | 4 | | | Roswell, N. Mex., October, 1921. | Not sick | Animal refused to eat after two feedings. |
| 671 | 36.75 | do | Milk from mother, No. 641. | | | | | | do | Weighed 36.5 pounds when turned out. |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| 668 | 91.5 | June 25–June 28, 1922 | With hay | Leaves | 1 | | | Roswell, N. Mex., October, 1921. | do | Refused to eat after two days. Weight when turned out was 78.5 pounds. |
| 678 | 89.5 | June 25–Aug. 26, 1922 | do | Stems, leaves, and flowers. | 31.48 | 17 | .5 | do | Sick | Kept quiet and not exercised. |
| 676 | 85 | July 3–July 9, 1922 | do | Leaves | .5 | | | do | Not sick | Refused to eat Aplopappus after two days. |
| 694 | 139 | Aug. 3–Sept. 1, 1922 | do | Stems, leaves, and flowers. | 19.8 | 14.52 | .66 | do | Sick | Symptoms on Sept. 2. Turned into pasture. |
| 686 | 133.5 | Aug. 3–Aug. 6, 1922 | do | do | .5 | | | do | Not sick | Refused to eat after first feeding. |
| 682 | 96.5 | Aug. 23–Aug. 31, 1922 | Balling gun | Leaves | 16.87 | 16.87 | 1.87 | do | Very sick | Given all the bran he would eat and kept quiet. |
| 677 | 107.5 | Sept. 13–Sept. 17, 1922 | do | do | 11.25 | 8.75 | 2.19 | do | Sick | Do. |
| 657 | 94 | Sept. 20, 1922 | do | do | 6.25 | 6.25 | | do | do | Feeding in one day; symptoms four days later. |
| 706 | 110 | Nov. 13–Nov. 18, 1922 | do | do | 11.25 | 11.25 | 1.87 | do | Death | Remedy, raw linseed oil. |
| 705 | 115.5 | Nov. 13–Dec. 22, 1922 | do | do | 18.75 | 18.75 | .47 | do | Sick | |
| 731 | 72 | June 22–July 16, 1923 | do | Stems and leaves | 50 | | | Roswell, N. Mex., May, 1923. | Not sick | |
| 771 | 16.75 | do | Milk from mother, No. 731. | | | | | | do | |
| 751 | 89 | June 21–July 15, 1923 | Balling gun | Stems and leaves | 50 | | | Roswell, N. Mex., May, 1923. | do | |
| 776 | 14 | do | Milk from mother, No. 751. | | | | | | do | |
| 716 | 72.5 | Aug. 8–Aug. 27, 1923 | Balling gun | Stems and leaves | 36 | 36 | 1.8 | Roswell, N. Mex., May, 1923. | Sick | |
| 743 | 72 | July 22–Aug. 20, 1923 | do | do | 60 | 60 | 2 | do | do | |
| 747 | 74 | July 22–Aug. 3, 1923 | do | do | 26 | | | do | Choked to death | |
| 711 | 68 | Sept. 17, 1923 | do | Stems, leaves, and flowers. | 6.25 | | | Roswell, N. Mex., October, 1921. | Not sick | |

### TYPICAL CASE OF STEER NO. 851

Steer No. 851 may be considered a fair type of all the cases. This was a steer received at the corrals in Roswell, N. Mex., October 19, 1919. He was a long yearling Hereford, healthy, but not in very good flesh, weighing 350 pounds. He received nothing to eat until 6.34 p. m., October 21, when some hay was given. Observations of temperature, pulse, and respiration were commenced at 6.30 p. m., October 21, and continued regularly twice a day during the course of the experiment.

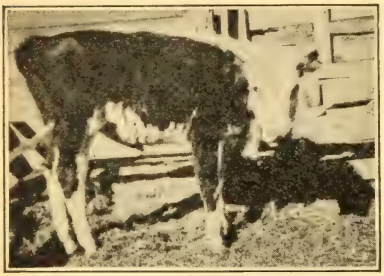

FIG. 3.—Steer No. 851 at beginning of experiment

The feeding of Aplopappus was commenced October 22 at 10.30 a. m. and was continued until results were obtained. Figure 3 shows the animal at the beginning of the experiment. The material fed consisted of stems, leaves, and matured flowers chopped up and mixed with a small quantity of alfalfa hay. The animal was given all the Aplopappus he would eat and only hay enough to induce him to take the Aplopappus.

On October 24, 27, and 29 he was exercised by being driven back and forth in an inclosure of 15 by 75 feet. On October 24 he was kept walking or running for 40 minutes and on October 27 for 20 minutes. It was noted on October 27 that the animal spent most of the time lying down. On the morning of October 28 he stood humped up and was stiff when walking.

On October 29 from 9.45 to 10 a. m. he was exercised in the same inclosure as before. He was slow in his movements and there was some trembling of the muscles of the shoulders and neck. Respiration was irregular. At 10.25 the animal was down but was helped up, and then would move only when pushed. He went down again and exhibited more pronounced trembling. The urine was colorless and the feces soft. During the rest of the day he was lying down most of the time, and when made to get up would immediately lie down again. Figure 4, taken at 10.26 a. m., shows the "humped-up" attitude assumed on October 28 and 29.

FIG. 4.—Steer No. 851 on October 29, showing "humped-up" attitude of sick animal

October 30 at 7 a. m. the animal was lying down and in the same position as at 9.45 the evening before. He got up at 7.45, but lay down directly, exhibiting distinct trembling in the shoulders and neck. The feces were becoming hard and showed blood and mucus. At 4 p. m. he was helped to his feet and stood eating hay for about

five minutes, when his shoulder muscles began to shake violently and he lay down. The trembling ceased after he lay down.

October 31 at 8.22 a. m. he was helped to his feet and began to eat, grating his teeth. He stood for about five minutes, then went down, being too weak to stand. He was down during the day, occasionally grating his teeth. At 5 p. m. he got up, was pushed to the watering trough, and drank a large quantity, then lay down again. Figure 5, taken at 4.45 p. m., shows the general condition at that time.

FIG.—5.—Steer No. 851 on October 31, 4.45 p. m.

November 1 at 10.30 a. m., by the use of an electric prodding pole, he was made to get up and move about the corral. After going around five or six times he fell to his knees and then lay down. While standing the muscles of the shoulders, forelegs, and neck trembled, and when driven about he bellowed.

November 2 at 11.32 p. m. he attempted to walk, staggered a few feet, and fell. When lying down he held his head extended, with nose resting on the ground. This attitude is shown in Figure 6, a picture taken at 11 a. m.

November 3 at 3.39 p. m. he attempted to get up and fell over on his side, but with help was able to right himself. At 5.40 he was on his side. The pulse during the day was rapid most of the time but the rate of the respiration was normal. After this he did not get up but remained on his side, and died at 12.43 p. m., November 4, without struggling.

FIG. 6.—Steer No. 851 on Nov. 2, 11 a. m.

In this animal the temperature remained normal during the course of the illness, but in others there was a drop shortly before death.

In the autopsy, which was made immediately after death, the heart was found in diastole. There was congestion in the fourth stomach, the duodenum, the jejunum, the ileum, and the rectum. The liver was pale, the bile dark and viscid. The left kidney and left lung were congested. The brain was congested and the blood vessels of the spinal column full.

### TYPICAL CASE OF SHEEP NO. 589

Sheep No. 589 (fig. 8) was a yearling wether which had been received at the experiment station June 5, 1920, and kept in the pasture.

June 20, 1920. The animal was kept in the corrals, and weighed at that time 85 pounds. He was kept under observation and nota-

tions were made in regard to temperature, pulse, and respiration. The animal was fed hay until June 25.

June 25. The experimental feeding of *Aplopappus heterophyllus* was commenced. The material was stems and leaves which had been collected near Roswell, N. Mex., in January, 1920. It was planned to give the animal approximately 2 pounds of green plant per hundredweight of animal daily. With the first feeding of Aplopappus was mixed 1 pound of alfalfa hay. The succeeding feedings were in practically this ratio, the attempt being made to have the animal, if possible, eat its full 2 pounds of Aplopappus daily. As a control, sheep No. 587 was kept in the corrals during the same time, was fed alfalfa hay, and given the same exercise. The feeding was continued until July 1 without anything unusual being noticed.

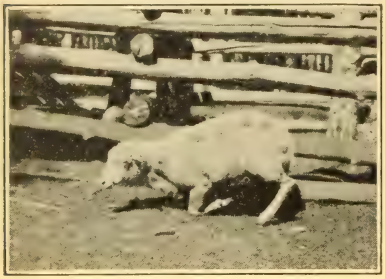

FIG. 7.—Sheep No. 373 showing extreme weakness; it could stand only a minute or two before it trembled and fell

July 1. While being exercised sheep No. 589 showed itself less active than the control, sheep No. 587. When placed back in the pen, sheep No. 589 immediately lay down, while sheep No. 587 remained upon its feet and commenced eating hay. Nothing more was noticed until July 3.

July 3. Both sheep were again exercised. While sheep No. 587 remained active and showed no indications of weakness, sheep No. 589 after a few minutes began to lag and showed a great disinclination to move about with any rapidity.

July 7. When exercised with sheep No. 587, sheep No. 589 lagged continually and soon stood still in the corner of the corral, refusing to move except under distinct urging. The animal continued quiet and stupid during the time from July 8 to 12.

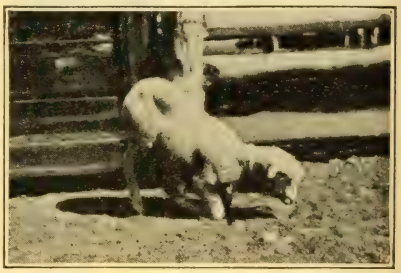

FIG. 8.—Sheep No. 589, July 17, when so sick that it trembled and fell after being on its feet only a few minutes

July 12. While the sheep was standing at the feed box in the morning it was noted that the shoulders were trembling. He walked across the corral with his back humped up and feet drawn under him, trembling violently in the shoulders and less markedly in the hips, and lay down. In a minute or less he was upon his feet and walked about normally. Immediately the trembling commenced again and he was obliged to lie down. This was repeated several times, although later in the forenoon he no longer exhibited trembling.

July 13. When exercised by being driven about the corral, he moved in a stiff-legged manner and was very stupid, but did not show trembling.

July 14 and 16. His condition remained about the same during these days. No trembling was noted, although the animal was stupid and inactive.

July 17. While being weighed in the morning, he commenced to tremble violently. The trembling was so severe that he was unable to stand upon his feet. These spells of trembling were repeated several times. Figure 8 shows this animal at 9.48 a. m.

July 18. When observed during the forenoon he exhibited periods of trembling and extreme weakness as on the preceding days.

July 19. The condition of the animal remained the same with no marked symptoms except the trembling and weakness.

July 21. At 8.45 a. m. the animal was very quiet and stupid, standing in a humped-up position. When observed in the afternoon at 4.38 p. m. he was trembling and was unable to remain upon his feet more than two or three minutes at a time.

July 22. At 6.45 a. m. he was found lying stretched out on the right side. He was raised to his feet and stood for a few seconds and then began to tremble. The trembling grew very violent and he lay down, falling on his right side. After a few deep breaths he died, at 6.49 a. m.

This animal was made sick in 17 days of feeding, receiving in that time 22.82 pounds, and, after the first symptoms appeared, ate 8.47 pounds of Aplopappus. An autopsy was made immediately after death. Regular observations of temperature, pulse, and respiration had been made, but nothing abnormal was noticed in these particulars except a high rate of respiration at 4.38 p. m., July 21, when he was breathing 132 times a minute. The only marked symptoms in the course of the illness were the weakness, stupidity, and trembling.

## DISCUSSION AND GENERAL CONCLUSIONS

### SYMPTOMS

*Depression and weakness.*—The first effect noticed in poisoned animals is marked depression. The animals are inactive, appear stupid sometimes, particularly in the cases of the sheep, stand "humped up," and move with a more or less stiff gait. The "humped-up" position is shown in the picture of steer No. 851, Figure 4. The stiffness and weakness are more pronounced in the forelegs. In cattle Nos. 892 and 840 this was shown very clearly, for when somewhat wearied by exercise they would come down on their knees and sometimes even attempt to move along in this position. A picture of sheep No. 589 in this position is shown in Figure 8. This inactivity gradually increases and culminates in extreme weakness, the animals in the later stages lying down most of the time, and eventually, in the more serious cases, being unable to rise. Figure 7 shows that condition of weakness in sheep No. 373; Figure 6 shows a more advanced case in steer No. 851; and Figures 9 and 10 show cow No. 868 in the last stages.

*Constipation.*—Constipation is present in most cases, but may be preceded or followed by a period of diarrhea. In the later stages the feces are not only hard but bloody.

*Urine.*—The urine is generally very light in color, and the animals, when exercised, frequently have an almost continuous dribbling of the urine

*Temperature.*—The temperature remains practically normal during the most of the illness, but in some fatal cases there was a marked fall shortly before death.

FIG. 9.—Cow No. 868 showing extreme depression and weakness

*Respiration.*—The respiration in the sick animals a short time before death was very characteristic. It was labored, a prolonged inspiration being followed by a pause and then a short and somewhat forcible expiration. In still later stages the animal breathed in a series of gasps.

*Trembling.*—Trembling is almost always present and may be considered a diagnostic symptom. This is recognized by the stockmen, who sometimes call the disease "the trembles." This varies from a slight twitching of the muscles, most commonly in the fore quarters, to a violent shaking of the whole body. These periods of trembling are brought on by exercise and are liable to continue until the animal gets down and has a period of rest. In some of the cases the breath of the animal had a distinct odor of acetone.

*Death quiet.*—Some of the animals kicked about a little before death, but did not have distinct spasms, and more frequently died without struggles. In some of the fatal cases the animals lay in a condition of coma for a considerable period before death.

### EXAMINATIONS OF URINE

Analyses of urine were made by J. F. Couch, chemist of the Pathological Division, cooperating in poisonous-plant investigations, in a number of the Aplopappus cases. Table 2 gives the detailed data of these examinations.

The total number of samples analyzed was 20, and comprised specimens from 13 cases. Six of the specimens were from cattle and 14 from sheep. All these animals had given evidence of Aplopappus poisoning before the samples were collected. Three samples were collected at autopsy; 7 samples were obtained by penning the animal in the metabolism cage during 24 hours (in one case 48 hours), and the remaining 10 samples consisted of one voiding each.

FIG. 10.—Cow No. 868 just before death

The data show the following significant facts. Twelve of the samples, or 60 per cent, were acid in reaction. Five gave positive tests for albumin. There was but one positive test for sugar. Fourteen of the samples were tested for the presence of acetone; 13 samples reacted positively, and only 1 was negative. Thus in 92.86 per cent of the tests acetone was found.

In general, then, it may be said that the urine from animals sick with Aplopappus poisoning will very probably be acid in reaction,

and is almost sure to contain acetone. Albumin and sugar will be found only if there have been extensive kidney lesions. They are by no means frequent, but their absence does not argue against a diagnosis of Aplopappus poisoning.

The urine findings point to a condition of acidosis.

TABLE 2.—*Summary of analyses of urine from Aplopappus cases*

| Animal | Date | Volume | Reaction | Specific gravity | Albumin | Sugars | Acetone | Urea | Remarks |
|---|---|---|---|---|---|---|---|---|---|
| Cattle Nos.: | | *Mls.* | | | | | | *Gms.* | |
| 840 | Sept. 10, 1920 | 155 | Alkaline | 1.032 | 0 | 0 | Not tested for. | | 1 voiding. |
| 840 | Sept. 14, 1920 | 490 | Acid | 1.027 | 0 | 0 | do | | Do. |
| 895 | do | 575 | do | 1.032 | 0 | 0 | do | 39.67 | 24-hour sample. |
| 924 | Sept. 7, 1921 | 880 | do | 1.020 | + | + | + | 19.69 | Collected at autopsy. |
| 961 | Aug. 26, 1922 | 1,640 | do | 1.022 | + | 0 | + | | Do. |
| 962 | do | 50 | do | | | | + | | Do. |
| Sheep Nos.: | | | | | | | | | |
| 589 | July 18, 1920 | 1,475 | do | 1.013 | 0 | 0 | Not tested for. | | 24-hour sample. |
| 563 | Sept. 5, 1920 | 1,105 | Alkaline | 1.010 | 0 | 0 | do | 10.04 | Do. |
| 570 | Sept. 9, 1920 | 365 | do | 1.046 | 0 | 0 | do | 22.89 | Do. |
| 676 | Aug. 13, 1922 | 60 | Acid | 1.033 | 0 | 0 | + | | 1 voiding. |
| 676 | do | 60 | do | 1.049 | 0 | 0 | + | | Do. |
| 676 | Aug. 14, 1922 | 60 | Alkaline | | 0 | 0 | + | | Do. |
| 676 | Aug. 15, 1922 | 80 | Acid | 1.022 | 0 | | + | | Do. |
| 676 | Aug. 16, 1922 | 100 | do | 1.023 | + | 0 | + | | Do. |
| 676 | do | | Alkaline | | + | | + | | Do. |
| 678 | Aug. 11, 1922 | 1,050 | do | 1.019 | 0 | 0 | + | | 24-hour sample. |
| 678 | Aug. 29, 1922 | 1,275 | Acid | 1.011 | 0 | 0 | Traces | 28.81 | Do. |
| 698 | Aug. 3, 1922 | 230 | do | 1.017 | 0 | 0 | + | | 1 voiding. |
| 701 | July 11, 1922 | 5 | Alkaline | | + | | + | | Do. |
| 634 | July 17, 1922 | 145 | do | 1.049 | 0 | 0 | 0 | | 48-hour sample. |

### AUTOPSY FINDINGS

Autopsies were made on 1 horse, 9 cattle, and 4 sheep. The results of the autopsies were not especially marked, but they were very uniform.

The heart was generally found in diastole. There was ordinarily more or less congestion in the fourth stomach, duodenum, jejunum, ileum, cecum, and rectum. This congestion in some cases was slight, and sometimes was only in spots, but was always present to a greater or less degree. The spleen was usually more or less congested, and the pancreas showed an abnormal quantity of blood in a number of cases. The liver was generally pale. The bile was usually thick, dark, and viscid, and the gall bladder was distended. The kidneys were congested in same cases, but ordinarily presented no abnormal appearance except that which would be expected from hypostasis.

The brain was congested in six cases, and in four the blood vessels of the spinal canal were unusually full. It could not be said, however, that this condition of the brain and spinal cord was a general occurrence.

In two cases an odor of acetone was noted in the abdominal cavity, and the presence of acetone was demonstrated by chemical tests conducted by J. F. Couch.

### MICROSCOPIC CHANGES IN TISSUES

In the autopsies certain changes were noted in various organs, these being usually related to alterations in the blood supply in the different tissues.

In the microscopic study the most noticeable changes were seen in the liver, kidneys, and blood.

*Liver.*—The livers in all cases, except that of the horse, were fatty. The quantity of fat varied considerably in different animals, but it was of the same character in all and consisted of fine and large fat globules in practically all the hepatic cells. In the most pronounced cases practically the entire cell body was taken up with the fat, the nucleus and remaining cytoplasm being pushed to one side. In most instances the fat was evenly distributed throughout the lobule. The hepatic cells of the horse's liver were not fatty but contained large quantities of pigment. The cells in most cases were more or less swollen, the cytoplasm often coarsely granular, and the nuclei frequently very variable in size and sometimes shrunken or irregular in outline. Not uncommonly there were somewhat excessive numbers of leucocytes throughout the intralobular capillaries, these having in some cases invaded the degenerated hepatic cells. There was wide variation in the quantity of blood present within the lobules in the different animals, apparently depending on the extent to which the hepatic cells were swollen.

In addition to the degenerative changes in the hepatic cells there was an effect on the bile ducts. The small ducts in several cases were distended, giving the epithelium a low, flattened appearance. In some cases the cells were swollen and granular or vacuolated; less frequently some cells were exfoliated or necrotic. The connective tissues surrounding such ducts was more or less congested and edematous and had become infiltrated with leucocytes.

This injury extended to the gall bladder, where it appeared in a more severe form. In the five cases sectioned, necrotic changes had occurred. Usually the epithelium had disappeared and the necrotic changes had extended to the other layers. Usually, too, congestion was pronounced, and in one case polymorphonuclear leucocytes were present in marked excess. These conditions are presumably associated with the bile changes noted at the autopsies and perhaps both have a bearing on the marked accumulation of pigment in the liver of the horse.

*Kidney.*—More or less injury to the kidney parenchyma was present in all the animals. This was most marked in the convoluted tubules and consisted of a well-marked swelling and granular degeneration of the tubule epithelium. In the most pronounced cases this granular cytoplasmic material largely filled the lumina of the tubules, and there was more or less disarrangement of the nuclei and loosening of the cells from the basement membrane. In many instances casts were present. These as a rule were hyaline in appearance, but some contained exfoliated epithelial cells.

In a majority of the cases some at least of the glomerular tufts were congested, or even hemorrhagic. Usually the congestion was accompanied with edema, and often the epithelial cells, both of the glomerular tufts and the capsule of Bowman, were swollen or granular.

Congestion of the other portions of the kidney was not constant, but usually in each section individual or groups of injected capillaries or minute hemorrhages were present.

*Blood.*—Evidences of degenerative changes in the red blood corpuscles were present throughout the various tissues, though they appeared most prominently in such organs as the spleen, liver, kid-

neys, and lungs. As a rule the erythrocytes did not take the stains strongly, and very often faintly stained, swollen, and distorted forms were present in considerable numbers. In the veins of the liver there was an abundance of granular débris, some of which appeared to be the remains of degenerated erythrocytes. In some lymph glands erythrocytes in considerable numbers were within phagocytic cells.

In addition to the degenerated red blood corpuscles, hematogenous pigment in considerable quantities was present in various places. This was often free in the blood stream, but nearly as frequently was found within phagocytic cells or imbedded in such tissues as the epithelial cells of the kidney tubules or the parenchyma of the liver. Less often it was in the walls of arteries and other places.

Evidences of injury to the walls of the blood vessels were not so apparent as were those of degeneration of the red blood corpuscles.

*Heart.*—The changes in the walls of the ventricles were not so advanced as in the tissues mentioned above. In half of the cases there were small areas of capillary congestion, and often minute hemorrhages. In none of the cases did the cross striation of the muscle fibers stand out well. Many fibers, scattered or in groups, had taken the eosin stain strongly, and some were very uniformly stained and their nuclei more or less shrunken. In such areas fine granular pigment particles were often present.

*Alimentary tract.*—Little was found in the various portions of the alimentary tract to warrant general conclusions. In some instances the various portions of the intestines were congested, accompanied with edema. This condition was somewhat more marked in the ileum than in other portions. Taken as a whole, there was an apparent increase in and swelling of the cellular elements of the interglandular tissues of the mucosa and often an invasion of the submucosa by leucocytes. In the horse, phagocytic cells containing red blood corpuscles were abundant in both the mucosa and submucosa of the various portions of the intestines.

*Lymph glands.*—A condition present in the mesenteric lymph glands was perhaps related to the disturbance in the intestinal walls. Almost invariably the lymph spaces in these glands were occupied with swollen and often more or less degenerated endothelial leucocytes, which usually contained engulfed red blood corpuscles or the products of their degeneration. In addition the branched reticular cells were swollen and sometimes contained granules of hematogenous pigment.

A similar condition but less marked was found in the posterior mediastinal lymph glands. In some instances in both groups as well as in other lymph glands, minute hemorrhages were found. These were not characteristic of lymph glands, however, but were found in other places.

*Spleen.*—A well-marked passive congestion was usually found in the spleen, accompanied with edema of the Malpighian bodies. Frequently the large mononuclear cells were present in abundance in the spleen pulp and hematogenous pigment was present in considerable quantity.

*Pancreas.*—The veins and capillaries of the pancreas were somewhat distended and usually there was a slight edema. As a rule the ducts were more or less distended and contained considerable

secretion. This was frequently associated with the presence of considerable zymogen in the acinar cells.

Summarizing this work, it appears that the most noticeable changes were degeneration and fat accumulation in the liver parenchyma with degeneration of the bile ducts and gall bladder; well marked, but not extreme, parenchymatous nephritis in the kidneys, and degenerative changes in the red blood corpuscles. In the heart muscle there were less severe degenerative changes than in the preceding tissues. The changes in the walls of the alimentary tract were mild in character but indicated the presence of a mild irritant. The changes in the other organs were apparently secondary in character to those indicated.

### TOXIC DOSE FOR SHEEP

In a discussion of the toxic and lethal dosage, inasmuch as the figures are based on the green weight of the plant, it is necessary to consider the loss of moisture in the drying of the plant. The last two cases, sheep Nos. 716 and 743, were given plants collected in May, when the loss in drying was 75 per cent. The rest of the experiments were with plants collected in the fall and early winter when the loss by drying was 50 per cent.

Of all the cases of poisoned sheep in which the fall and early winter plants were used the smallest dosage was 6.25 pounds per 100 pounds of animal in sheep No. 657. This was given by balling gun in a single day, but the symptoms did not appear until four days later. The largest quantity necessary to produce symptoms was 36.82 pounds per 100 pounds of animal in the case of sheep No. 576, the feeding being extended over 29 days. The daily feeding varied from 0.47 to 6.25 pounds per 100 pounds of animal. This last case, however, was exceptional, as the attempt was made to force into the animal as large a quantity as possible in one day. The average of the other daily feedings was 1.17 pounds per 100 pounds of animal. Most of the daily feedings were not far from this average, as this quantity was about all that a sheep could take in a single day. Averaging all these experimental sheep, the total feed per 100 pounds of animal to produce illness was 23.25 pounds given in 19.5 days, the average daily ration being 1.19 pounds.

Put in a general way, sheep are poisoned on a daily feeding of about 1.25 pounds per 100 pounds of animal continued for about three weeks, although they may be poisoned in a week or less.

### TOXIC AND LETHAL DOSAGE

In Table 3 are gathered together the data in regard to the toxic and lethal doses for the animals which were affected by the plant.

None of the experimental sheep which received 1.5 pounds per 100 pounds of animal daily failed to be poisoned, with one exception: Sheep 495 received 1.9 pounds daily for 51 days with no symptoms. This animal was kept constantly in good pasture.

Of the two sheep, Nos. 716 and 743, poisoned on the spring plants, the average to produce illness was 48 pounds per hundred weight of animal given in 25 days, with an average daily dosage of 1.9 pounds. Reduced to dry weight, this would be 12 pounds and an average daily dosage of 0.475 pound given in 25 days. A similar reduction to dry weight of the cases fed on fall and early winter plants would

TABLE 3.—*Toxic and lethal dosage*

| Designation | Method of feeding | Part of plant fed | Per cent of animal weight to produce illness, estimated as green plant | Time fed to produce illness | Average percentage of green plant fed daily to produce illness | Result |
|---|---|---|---|---|---|---|
| Cattle Nos.: | | | *Per cent* | *Days* | *Per cent* | |
| 851 | With alfalfa hay | Stems, leaves, and flowers. | 9.428 | 7 | 1.347 | Death. |
| 853 | do | do | 8.85 | 6 | 1.47 | Do. |
| 854 | do | do | 17 | 8 | 2.125 | Do. |
| 856 | do | do | 9.648 | 8 | 1.206 | Do. |
| 855 | do | do | 46.82 | 34 | 1.377 | Do. |
| 892 | do | do | 9.742 | 5 | 1.948 | Recovery. |
| 840 | do | do | 15.46 | 8.5 | 1.819 | Do. |
| 868 | do | do | 22.46 | 11 | 2.04 | Death. |
| 961 | do | do | 16.06 | 11 | 1.46 | Do. |
| Horses Nos.: | | | | | | |
| 132 | do | do | 15.21 | 18 | .845 | Do. |
| 133 | do | do | 17.852 | 18 | .992 | Sick, partial recovery but no record of final outcome. |
| Sheep Nos.: | | | | | | |
| 589 | do | do | 12.048 | 8 | 1.50 | Death. |
| 563 | do | do | 33.94 | 35 | .97 | Recovery. |
| 576 | do | do | 36.82 | 29 | 1.27 | Do. |
| 373 | do | do | 25.32 | 19 | 1.33 | Do. |
| 701 | Balling gun | do | 28 | 17 | 1.64 | Death. |
| 678 | With alfalfa hay | do | 17 | 34 | .5 | Recovery. |
| 694 | do | do | 14.52 | 22 | .66 | Do. |
| 682 | Balling gun | Leaves | 16.83 | 9 | 1.87 | Do. |
| 677 | do | do | 8.75 | 4 | 2.19 | Do. |
| 657 | do | do | 6.25 | 1 | 6.25 | Do. |
| 706 | do | do | 11.25 | 6 | 1.87 | Death. |
| 705 | do | do | 18.75 | 40 | .47 | Recovery. |
| 716 | do | Stems and leaves | 36 | 20 | 1.8 | Do. |
| 743 | do | do | 60 | 30 | 2 | Do. |

give to produce illness 10.25 pounds, given in 19 days with a daily dosage of 0.54 pound. It would appear that, on the basis of dry weight, taking into consideration the number of days fed, there is little difference in toxicity between the two sets of collections.

*Fed cases of sheep compared with balling-gun cases.*—To some of the sheep the plant was given with balling gun, while for others it was mixed with hay. The latter, presumably, would consume more time in eating a given quantity of plant and it might be expected that the toxic result would not appear quite so quickly. A comparison of the experiments, however, shows that this was not the case. On the average there was very little difference between the balling-gun and the fed cases.

### TOXIC DOSE FOR CATTLE

It will be seen from Table 3 that cattle may be made sick in as short a period as five days, this being on a daily dosage of very nearly 2 pounds per 100 pounds of animal. The smallest daily feeding which produced poisoning was 1.206 pounds per 100 pounds of animal, which made No. 856 sick in eight days. The total quantity to produce sickness varied from 8.85 pounds per 100 pounds of animal in No. 853 to 46.82 pounds per 100 pounds of animal in No. 855.

Averaging all the cases which were made sick, the feeding of 1.64 pounds daily for 10.93 days produced sickness; or, putting it in a general way, if cattle receive 1½ pounds of the plant daily they may be expected to be made sick in about 11 days.

### TOXIC DOSE FOR HORSES

Only two horses were used. With these animals the poisonous effect on the average was produced by a feeding of 0.918 pound per 100 pounds of animal, continued for 18 days.

### LETHAL DOSE

The experiments give no definite indications of the lethal dose, as compared with that necessary to produce intoxication. Some of the animals died with no further administration of the plant after symptoms appeared. Others received additional quantities of the plant. But the data do not make it clear that in the fatal cases there was any definite increase over the toxic dose.

Generally speaking, the prognosis of cases in which marked symptoms of poisoning occurred was not good. Recoveries did occur under favorable circumstances, but one would rather expect a fatal termination of the serious cases.

### COMPARISON OF TOXIC DOSES IN CATTLE, SHEEP, AND HORSES

Inasmuch as in a general way cattle are made sick in 11 days by eating 1.5 pounds daily per 100 pounds of animal, and sheep are made sick by eating 1.25 pounds daily for 3 weeks, it would appear that cattle are somewhat more susceptible to the poisonous effects of Aplopappus than are sheep. The horses were made sick on a still smaller daily dose, about 1 pound per 100 pounds of animal, in 18 days. Since the result on horses was from only two animals, it can not be considered as being so exact as the results on the considerable number of sheep. So far as the experiments go, however, it may be thought probable that horses are more easily affected than cattle.

In this connection it may be noted that although the dosage of cattle was smaller than that of sheep, there were more recoveries of sheep. Of the sick animals, only 2 of the 9 cattle survived, while 11 of the 14 sheep recovered.

### DURATION OF SICKNESS

Many of the data in regard to the animals that recovered from the Aplopappus poisoning were far from exact. Not only was it difficult to state definitely when animals had recovered, even if under constant observation, but in many cases the animals were turned back to the owners before complete recovery had taken place.

In most cases, in order to get a more pronounced effect, the plant was fed for a considerable period after symptoms appeared. With some few animals there are definite data in regard to the time during which symptoms continued after they were first observed.

Although there is reason to think that sometimes recovery takes place only after a prolonged period, it seems clear that animals may come back to a condition nearly or quite normal in from one to two weeks after the feeding ceases.

Table 4 gives the time between the first recorded symptom and death in the case of animals that died.

TABLE 4.—*Time elapsing between the appearance of symptoms and death*

| Animal | Days | Hours | Minutes | Animal | Days | Hours | Minutes |
|---|---|---|---|---|---|---|---|
| Cattle Nos.: | | | | Cattle Nos.—Contd. | | | |
| 851 | 7 | 4 | | 961 | 8 | 6 | |
| 853 | 6 | | 10 | Horse No. 132 | 4 | 3 | |
| 854 | 4 | | | Sheep Nos.: | | | |
| 855 | 15 | 17 | | 589 | 21 | | |
| 856 | 7 | 1 | | 701 | 3 | 12 | 30 |
| 868 | 8 | 3 | 34 | 706 | 6 | 21 | 10 |
| 924[1] | 4 | [1] 11 | | | | | |

[1] Received milk of cow 868.

It will be seen that the time before death during which the animals were sick was very variable, the shortest period being 3 days and 12 hours, and the longest 21 days. The average of all cases was 8 days and 36 minutes. Of the 12 cases 4 exceeded 8 days of sickness, 4 were between 6 and 8 days, and 4 were between 3 and 5 days. The plant can hardly be considered as causing acute poisoning. An animal may linger for nearly 3 weeks, but may be expected to die in about a week.

### APLOPAPPUS A CUMULATIVE POISON

It is evident that Aplopappus is a cumulative poison. There is some elimination, but it is not sufficient to prevent poisoning even when the plant is fed in very small quantities. Sheep Nos. 705, 678, and 694 exhibited symptoms on daily quantities varying from 0.47 to 0.66 pound per hundredweight of animal. This indicates little elimination.

### TRANSMISSION OF THE POISON BY MILK

There is a widespread belief among stock people of the Pecos Valley that animals giving milk may transmit the alkali disease through the milk to their offspring, producing diseased calves and lambs, and that human beings using the milk or butter suffer from the same disease, which in their case is most commonly known as milk sickness. It is also stated by many that the poisonous substance is excreted through the milk to such an extent that the mothers show no symptoms, but the offspring are poisoned.

A number of experiments were made to show whether or not this was the case. Table 5 summarizes the results of these experiments.

TABLE 5.—*Effect of plant upon milk-giving animals and their offspring*

| Cow No.: | | Calf No.: | | Ewe No.: | | Lamb No.: | |
|---|---|---|---|---|---|---|---|
| 840 | Sick | 895 | Probable symptoms. | 701 | Death | 700 | Death. |
| 892 | do | 893 | Symptoms. | 373 | Sick | 655 | Sick. |
| 911 | Not sick | 917 | Probable symptoms. | 495 | Not sick | 656 | Not sick. |
| 868 | Death | 924 | Death. | 731 | do | 771 | Do. |
| 961 | do | 962 | Not sick. | 751 | do | 776 | Do. |

It will be seen that in three cases neither the sheep nor the lamb was affected. Of the other cases cow No. 911 was not affected, but its calf, No. 917, exhibited probable symptoms. In one case, cow No. 961, the cow was affected, but not the calf. In five cases both the mother and the offspring were affected. In all these cases in which the calves or lambs were made sick the symptoms were typical of the alkali disease.

These experiments show very clearly that the poison may be transmitted to the offspring by the milk. They also show clearly that, while it is possible that the offspring may be affected without the mothers showing any symptoms, the poisonous substances are not in all cases, perhaps very seldom, excreted so completely as to prevent the exhibition of symptoms in the mothers.

These results have an important bearing on the use of milk and butter from herds affected by the alkali disease. The data at our command seem to show that the belief held by many people that it is dangerous to use milk or butter from such animals is well founded. There have been cases of human sickness that, to all appearances, were caused by the use of milk or butter from sick animals or from animals that were eating largely from the rayless goldenrod. It is difficult and perhaps impossible to get definite proof that cases of milk sickness in human beings have arisen in this way, because of the necessary limitation of experimental work on human beings. The results, however, are sufficiently definite so that it is reasonable to caution people against using, to any large extent, milk or butter from cows which either show symptoms of milk sickness or are grazing very largely on the rayless goldenrod.

During the winter of 1922–23 a very interesting series of cases of human milk sickness in the Pecos Valley was reported to the Department of Agriculture by W. H. Enneis, field agent of the United States Public Health Service. These patients showed all the typical symptoms ascribed to milk sickness. They had consumed large quantities of milk and butter from cows kept in pastures which contained little grass and much rayless goldenrod. A suckling calf kept with its mother in one of these pastures died with "trembles."

Tissues obtained from one of these human cases which terminated fatally were examined by Clawson, who has done the microscopic work on tissues of animals killed by Aplopappus, and found to correspond in pathological character to similar tissues from animals.

### EFFECT OF EXERCISE ON ANIMALS

In the experiments at Roswell four of the cattle and one of the horses were given exercise during the feeding work. This consisted in being driven back and forth in an inclosure, or, in the case of the horse, of being ridden. The exercise was of a rather severe character. Steer No. 855, which received no exercise before the appearance of the symptoms, lasted much longer than the others. Horse No. 133, which received no exercise before symptoms were noted, made a partial recovery; the other horse, No. 132, which was exercised, died and showed symptoms on a smaller dosage than No. 133.

In the succeeding work at the Salina experiment station similar results were noted, the periods of trembling following more or less severe exercise. The effect of the exercise was to precipitate the symptoms and probably, by using up the strength of the animals, to make them more liable to yield to the effect of the poisonous plant. It is a natural inference that in handling animals affected by the Aplopappus, recovery is more probable when the animals are kept as quiet as possible. In this connection it may be remarked that physicians and others who are familiar with cases of human milk sickness have often noted that symptoms are frequently brought

on or aggravated by severe exercise, and that patients well on the road to recovery sometimes have serious relapses as the result of more or less severe muscular exercise.

### EFFECT OF STERILIZED PLANT

Because of the theory held by some that the "alkali disease" is produced by bacterial infection it was thought best to feed some sterilized material. The plant was prepared by being autoclaved at 8 pounds pressure for 20 minutes, followed by 12 pounds for 17 minutes. Unfortunately, cultures were not made to prove the completeness of sterilization. Inasmuch, however, as with the means of heating—a primus burner—it took nearly an hour to get the initial pressure, the plant must have been pretty well penetrated by the steam, and it may be assumed perhaps that the sterilization was complete.

This plant material was fed to sheep No. 563 and produced the same effect as the untreated plant. So far as the evidence of this single experiment goes it tends to confirm the belief that the poisonous effect is produced not by bacteria but by the toxic principles of the plant.

### EFFECT OF EATING GRASS WITH THE APLOPAPPUS

Several of the animals received with the Aplopappus more or less grass. Sheep Nos. 566 and 495 were kept in pasture during the experimental feeding. Sheep Nos. 701, 563, and 373 and cattle Nos. 868, 892, and 840 received cut grass in the feeding pens.

Taken as a whole, these animals were not so readily poisoned as those that were kept on dry feed. Cow No. 892 became sick in the feeding pens and recovered while still eating Aplopappus and cut grass. Sheep No. 563, which became sick while eating Aplopappus and hay in the pens, recovered after being put on pasture.

The question of the effect of grass feeding is complicated by the fact that cattle Nos. 868, 892, and 840 and sheep Nos. 701, 495, and 373 were giving milk, and (as shown on page 22) more or less of the toxic substance is excreted in the milk. It was evident, however, that grass feeding tended to delay the production of symptoms and to aid in recovery, presumably owing to the laxative effect of the grass feeding.

Stock eat the rayless goldenrod only when confined to pastures where there is little good forage; hence the obvious remedy is to see that the animals are adequately fed.

### DESTRUCTION OF THE PLANT

Aplopappus grows in great luxuriance in some places, but apparently it is not extremely difficult to dig it out of pastures. J. C. Camp, of Pecos, Tex., stated to one of the writers in the fall of 1919 that he cleaned a pasture seven years before, and not only had no trouble with his livestock kept there since that time but only a few plants had appeared. The plants were dug out to a depth of 2 or 3 inches. Similar testimony was obtained from persons living near Carlsbad, N. Mex.

The writers have had no opportunity to perform experimental work in eradication, but it seems probable from the evidence they have obtained that not only is eradication from pastures practically possible but also that it is the best way of combating the trouble.

## SUMMARY

A disease of cattle, commonly known as "alkali disease" or "milk sickness," has long been known in the Pecos Valley of New Mexico and Texas. A disease of human beings commonly known as "milk sickness" also occurs in the Pecos Valley, and has generally been identified with the disease of animals.

The cause of this disease has been obscure. Some have thought it was produced by drinking alkali water; some have thought it due to a pathogenic organism; others have thought it caused by a poisonous plant, the rayless goldenrod (*Aplopappus heterophyllus*) being especially suspected.

"Milk sickness" or "trembles" has been known in the Central and Eastern States for more than a century. It has been shown, however, that most if not all cases of milk sickness in the East are caused by the plant *Eupatorium urticæfolium*, commonly known as white snakeroot.

The experimental work detailed in this bulletin has shown that cattle, horses, and sheep, when given sufficient quantities of rayless goldenrod, develop all the typical symptoms of alkali disease or milk sickness. The toxic doses have been determined and the conditions under which poisoning is liable to take place have been discussed.

It has been shown that the toxic substance may be excreted in milk, and that calves and lambs may be poisoned in this manner. It is probable that human cases of milk sickness arise from the consumption of milk or butter from cows feeding on the rayless goldenrod.

It is shown that stock eat the rayless goldenrod only when confined in pastures where there is little good forage, so that the obvious remedy is to see that the animals are well fed. It is entirely practicable also to dig out the weed in fenced pastures.


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